

REMARKS

Claims 1 to 5, 10 to 15, and 18 remain unchanged. These claims have been allowed.

Claims 6 to 9 and 16 have been amended. Claim 17 has been canceled. Accordingly, the rejections under the second paragraph of 35 U.S.C. 112 and the objection to claim 17 are moot and should be withdrawn.

The subject matter of claim 20 has been split into claim 20 and new claim 22. Claims 21 and 23 to 28 have been added and are directed to further specific disorders of the central nervous system. These disorders are disclosed in the application as originally filed, i.e., page 17, line 34 (neurodegenerative disorders), page 18, lines 17 and 37 (anxiety); page 18, line 13 (schizophrenia); page 18, line 1 (dementia), page 18, line 4, (cognitive disorders), page 18, line 3 (Alzheimers Disease), page 17, line 36 (ischemic event).

Claims 19 and 20 have been rejected under the first paragraph of 35 U.S.C. 112 as allegedly failing to comply with the enablement requirement. The Examiner contends that the specification does not enable the instant compounds to treat disorders of the central nervous system, a neuropsychiatric disorder or depression. We disagree for the following reasons:

The specification teaches that the claimed compounds have useful pharmaceutical properties. In particular, they have high affinity for 5-HT_{1B/D} and 5-HT_{1A} receptors (page 16, lines 10 and 11). More particularly, the specification teaches the binding affinities for the compounds described in Examples 4, 9, 13, 15, 16, 20, 21, 22, 24, 28, 31, and 32 (page 39).

The specification further teaches that compounds having high affinity for these receptors have already been proposed as active ingredients for a variety of neurodegenerative and neuropsychiatric disorders (page 2, lines 27-32).

The Office Action referred to Cryan et al. as allegedly showing a speculative nature of the role of serotonin (5-HT) receptors in the treatment of depression.

The Examiner's skepticism appears to be based on the following statement found on page 125, right-hand column of Cryan et al.:

"However, the key for the next generation of progress is to unravel the complex effects of activation/antagonism of the various post-synaptic 5-HT receptors and their significance, if any, in mediating the anti-depressant response."

We believe that said statement merely reflects some uncertainty about the ex-act mechanisms underlying the antidepressant response, but it cannot be taken as a general showing that the role of 5-HT receptors in the treatment of depression was speculative.

To the contrary, in Cryan et al. 2000, clinical studies with 5-HT_{1A} receptor ligands are described, which clearly showed a rapid and robust diminution of the depressed symptomatology (see, for instance, page 122, right-hand column, first full paragraph).

The criticism in Cryan et al. 2000 is that it cannot be determined if 5-HT transmission was indeed enhanced, despite the effectiveness seen in the clinical studies and the anticipation that arises from preclinical studies (see page 122, right-hand column, second full paragraph). It is against this back-ground that the statement upon which the Examiner is relying merely reflects the wish of unraveling the exact mechanism by which the drugs act.

There is a large body of literature that corroborates the usefulness of 5-HT_{1A} receptor ligands for treating a variety of CNS disorders. The following table is a listing of some helpful publications:

| Author, year | Target | Disorder |
|---------------------|--------------------|--|
| Schechter, 2002 | 5-HT _{1A} | Alzheimer Disease, cognitive dysfunction, depression, anxiety, drug and nicotine withdrawal, schizophrenia |
| Bantick, 2001 | 5-HT _{1A} | schizophrenia |
| Hjorth, 2000 | 5-HT _{1A} | depression |
| Davids, 1996 | 5-HT _{1A} | anxiety |
| Lutsep, 2005 | 5-HT _{1A} | ischemic stroke |
| Sato, 2007 | 5-HT _{1A} | dementia |

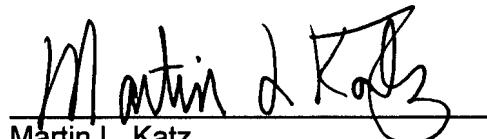
These publications show that the person skilled in the art would have been able to use the compounds of the present invention for treating disorders of the central nervous system without undue experimentation.

A copy of each of said references is attached hereto.

In view of the above remarks, withdrawal of the rejection of claims 19 and 20 and allowance of claims 6-9, 16 and 19-28 is respectfully requested.

Respectfully submitted,

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